

EDITORIAL COMMENT

Remote Monitoring and Outcomes in Pacemaker and Defibrillator Patients

Big Data Saving Lives?*

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Remote monitoring (RM) of cardiac implantable devices now enables daily monitoring and notification of device function and patient clinical status. Past guideline recommendations have endorsed in-person follow-up of device patients or RM every 3 to 6 months (1-3), but RM offers a simpler alternative, which surveys have shown patients prefer and physicians find straightforward to use (4,5). Large observational studies using data from RM follow-up databases of device manufacturers, involving >500,000 patients, have evaluated whether RM has a substantial impact on clinical outcomes including survival. These studies consistently show that RM is associated with a survival benefit compared with periodic in-person device follow-up. Smaller randomized clinical trials have shown less benefit or no significant survival difference.

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In this issue of the *Journal*, 2 studies shed considerable light on this important knowledge gap. Varma et al. (6) report findings from their observational cohort study of 269,471 patients implanted with pacemakers (PMs), implantable cardioverter-defibrillators (ICDs), and cardiac resynchronization therapy PM/defibrillators (CRT-P/-D) with RM capability (St. Jude Medical, Inc., Sylmar, California),

comparing outcomes in those who received only in-person follow-up with those who used RM. This study has several important findings. First, more than one-half (53%) of patients implanted with RM-capable devices never used the RM functionality. Second, there was a survival advantage for those patients who used RM, and increased use of RM with weekly transmissions more than 75% of the time was associated with a greater survival advantage compared with those who used RM less frequently. Finally, these results were consistent across all device types including PMs, ICDs, and CRT devices.

These findings are very consistent with those from the ALTITUDE (7) observational cohort study of 69,556 patients implanted with ICD and CRT-D devices (Boston Scientific Corporation, Natick, Massachusetts). This earlier study reported a 50% reduction in mortality (ICD hazard ratio: 0.56; CRT-D hazard ratio: 0.45; $p < 0.0001$) in those patients who used RM compared with those who had only in-person follow-up. Varma et al. (6) extend the results of the ALTITUDE study by showing that higher use of RM was associated with improved survival in a dose-response relationship. This finding may be particularly important in helping to understand why some previous studies with less frequent RM did not have a substantial impact on outcomes, such as survival. There may be a threshold of RM frequency beyond which outcomes are substantively impacted, with greater effect as RM frequency increases. Varma et al. (6) also extend the ALTITUDE results by demonstrating a survival benefit with RM-capable PMs with an effect size consistent with that for ICDs. This is important in that it may provide some insight into the putative mechanisms by which RM patients have improved outcomes. PM patients are generally less ill than ICD patients and the devices

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have fewer therapeutic and diagnostic functions capable of conferring a survival advantage. The authors hypothesize that the consistent effect size between PMs and ICDs suggests that identification and treatment of atrial arrhythmias, high-rate episodes, or changes in pacing and lead parameters may mediate the improved survival with RM devices. However, RM may also simply intensify physician and patient engagement and communication more generally, apart from specific device functionality.

The ALTITUDE study and the study by Varma et al. (6) are similar with regard to their observational study design. These studies have the great advantage of including very large patient cohorts that are highly representative of the larger population of U.S. device recipients and, therefore, generalizable relative to the more rarefied and selected clinical trial populations. These cohort studies are also similar in their limitations, including the fact that both had only modest data on baseline clinical characteristics that would have allowed for comprehensive adjustment for clinical differences between patients using RM and those treated with in-person visits only. RM use may serve as a marker for patients who are more fastidious about their health and physicians who are more intensive with their care, rather than a true mediator of improved outcomes. Alternatively, sicker patients may be referred for RM to allow closer follow-up and, in this scenario, RM-selected patients would be expected to have a survival disadvantage. The ALTITUDE authors performed a sensitivity analysis, which showed that baseline risk that had not been accounted for in the analysis would need to be 5 times greater in the patients not using RM to make the reported survival benefit nonsignificant, suggesting that the association between RM and survival is likely robust. All the patients evaluated by Varma et al. (6) in the present study were implanted with RM-capable devices, which should at least partially address the concern of confounding introduced by baseline patient differences. In addition, another observational cohort study (8) of 37,742 patients implanted with ICD and CRT-D devices (Boston Scientific) was recently presented and linked device RM data from ALTITUDE to detailed patient characteristics from National Cardiovascular Data Registry ICD Registry for improved patient characteristic analytic adjustment. This study showed an improvement in patient survival consistent with the previous observational studies. Nonetheless, it remains possible that residual confounding factors account for some of the reported association between RM and improved outcomes in these observational cohort studies.

Although a large prospective randomized clinical trial would control for the most likely confounding factors, a new trial is unlikely to be undertaken given that the technology for RM now exists in all devices at minimal or no extra cost.

Previous randomized controlled trials evaluating an association between RM and patient outcomes have been relatively small and have shown a benefit in some studies but no significant difference in others. One of the largest and the most contemporary of these studies was the IN-TIME (Influence of Home Monitoring on Mortality and Morbidity in Heart Failure Patients with Impaired Left Ventricular Function) trial (9), which included 664 ICD and CRT-D patients randomly assigned to either automatic, daily RM in addition to standard care or standard care alone. The primary outcome measure was a composite clinical score combining all-cause death, overnight hospital admission for heart failure, change in New York Heart Association class, and change in patient global self-assessment. At 1 year, 63 (18.9%) of 333 patients in the RM group compared with 90 (27.2%) of 331 in the control group ($p = 0.013$) had worsened composite scores (odds ratio: 0.63; 95% confidence interval: 0.43 to 0.90) and 10 versus 27 patients who died during follow-up. These contemporary data seem to confirm the observational study findings, but were discordant with several previous randomized studies.

In an effort to synthesize the currently available randomized controlled trial data and make sense of the disparate results, Parthiban et al. (10) also report in this issue of the *Journal* a systematic review and meta-analysis of 9 randomized controlled trials comparing RM with in-person follow-up in patients with cardiac implantable devices. They showed that across all 9 studies, including approximately 6,500 patients, there was no significant difference in all-cause mortality, cardiovascular mortality, hospitalization, or ICD shock, although there was a reduction in the risk of inappropriate shock and the time required to detect a clinical event or reach a clinical decision. However, importantly, in the 3 trials (including IN-TIME) that used daily RM transmission, there was a significant reduction in all-cause mortality, suggesting that the benefits of RM can only be fully realized with more frequent RM data transmission. Moreover, the mean follow-up interval in the randomized trials was significantly less than in the observational studies that continue to see benefit out to 5 years of follow-up.

Thus, the observational and randomized trial published data seem to consistently demonstrate that RM of patients with cardiac implantable devices is safe, with outcomes at least comparable with those

treated with in-person follow-up alone. Furthermore, contemporary studies suggest that with more frequent RM transmission (daily in the most recent studies) outcomes may be superior, including a possible survival advantage over periodic in-person device evaluation. In light of these results, the consistent finding in the observational published data showing that RM use remains poor in clinical practice suggests that efforts to change treatment patterns through more aggressive use of guideline recommendations and continuing medical education should be undertaken at this point. Additionally, research must be conducted to better understand patient- and physician-level impediments to adopting RM and methods to address these barriers. RM and remote patient engagement represent a cultural shift in the traditional medical care model and allow for a more fluid and continuous patient care paradigm that many physicians may not feel comfortable integrating into their practice behaviors. Nonetheless, digitally enabled remote diagnostics provide an incredible opportunity to use the efficiency of wireless network data collection and analytics to engage and benefit the implanted device population and realize more value from the device itself.

Finally, the cardiac implantable device and research communities should continue to investigate

ways of optimizing and improving RM and the timely use of “big data” to improve clinical outcomes. We need to improve artificial intelligence methods for automating triage of RM data that would minimize the need for practitioner review and prioritize more clinically important data to facilitate rapid clinical decision support and timely intervention. Data delivery directly to patients through an alert or Internet-based system could be developed that enables patients to better understand their clinical status and allows them to respond in a timely fashion; independently when appropriate, or with clinician input when necessary. RM data can be integrated with electronic medical records to ease clinician administrative burden and minimize the risk of data being lost or inaccurately recorded. Cardiac implantable devices are in the vanguard of the personal “big data” revolution; it is imperative that we continue to improve the quality and use of the data they generate to best meet the needs and optimize the outcomes of patients and enable physicians to practice most efficiently.

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